REMARKS

In the Office Action dated May 26, 2005, the Examiner rejected claims 1, 2, 5-18 and 22-45 as being anticipated by or unpatentable over Chang et al. (USPN 4,507,555) and/or Demirev et al. (Analytical Chemistry, Vol. 69, No. 15, pp. 2893-2900 (1997)), either taken individually or in combination. By this communication, Applicants have amended independent claims 1, 22, and 29 to more clearly distinguish the invention over the prior art. Support for the amendments may be found, for example, at page 8, lines 4-6 and page 14, lines 1-5 of the specification. Reconsideration of the claims as amended is respectfully requested.

Prior to discussing the specific rejections, Applicants offer the following summary of the Chang and Demirev references to assist the Examiner to understand how the disclosures of these references differ from the claimed subject matter of the present Application.

Chang teaches a mass spectrometer having dual mass analyzers for concurrent analysis of ions produced from a single sample. The problem solved by the Chang apparatus relates to the timing of mass selective scans performed by a mass spectrometer relative to the elution of analyte substances from a chromatography column or other separation device. According to Chang (col. 2, line 37 et seq.), prior art mass spectrometers suffered from poor mass resolution because the initialization of the mass scan was not timed to the appearance of a chromatographic peak. Instead, the prior art mass spectrometers performed repetitive mass scans at a rate sufficiently rapid to ensure that several scans are conducted across each chromatographic peak. Chang states that the rapid mass scan rate "brings with it the problem of deterioration of the mass spectrum detection sensitivity and spectra quality" (col. 3, line 40). The Chang apparatus addresses this deficiency by employing two mass analyzers operating in parallel that simultaneously analyze ion streams formed from a common sample. The first mass analyzer is operated in total ion current (TIC) or single ion monitoring (SIM) detection mode to detect the occurrence of a chromatographic peak, i.e., components eluting from the chromatographic column or other separation device. When a peak is detected, a mass scan is initialized by the second mass analyzer. Because the mass scan is timed to the appearance of the chromatographic peak, as determined by the first mass analyzer, the mass scans can be performed at a lower rate relative to the prior art repetitive scanning technique, thereby producing better mass resolution

and yielding better quality mass spectra. Furthermore, because the mass scans are only performed in connection with the chromatographic peaks, the loading of computing resources (storage and processing cycles) is substantially reduced.

It is important to note that although Chang refers to its apparatus and to prior art apparatus having a similar architecture as "parallel mass spectrometers", the term "parallel", as employed by Chang, denotes the use of two or more mass analyzers to concurrently analyze ions derived from a **single** sample. The parallel architecture of Chang enables higher sensitivity analysis of a single sample rather than concurrent analysis of multiple samples. As will be discussed in further detail below, nowhere does Chang suggest an array of multiple interconnected mass spectrometry systems wherein each mass spectrometry system analyzes a different sample.

Demirev teaches a set of statistics that can be utilized to characterize the diversity in a combinatorial library of peptides. Notably, Demirev fails to teach a method or apparatus for concurrent analysis of multiple samples. While Demirev refers to a "massively parallel" mass spectrometric method, the term "parallel" does not denote parallel (i.e., concurrent) analysis of multiple samples by an interconnected array of mass spectrometry systems. Instead, Demirev employs "parallel" to mean measuring multiple components (peptides) in a complex mixture of peptides contained in a single sample.

Turning now to the specific rejections, independent claim 1 was rejected under §103(a) as being obvious over Chang. Applicants respectfully traverse this rejection as applied to the amended claim. The Examiner asserts that it would have been obvious to use the mass spectrometer of Chang to analyze multiple samples. While this assertion may be true, claim 1 recites a parallel array of mass spectrometry systems wherein each mass spectrometry system "analyz[es] a different one of the multiple protein samples" derived from separation of a complex protein mixture. Assuming, arguendo, that the Chang apparatus can be considered to be a "parallel array of mass spectrometry systems", the individual mass spectrometry systems of Chang (i.e., first quadrupole mass filter 21, second quadrupole mass filter 25, and their associated ion extraction means and electronics) do not meet the aforementioned claim limitation. Instead, the two "mass spectrometry systems" of the Chang apparatus concurrently analyze ions formed from **a single sample**, as is described at col. 6, lines 4-30. If analysis of

multiple samples is to be performed using the Chang apparatus, such analysis must be performed serially, i.e., one sample at a time. As is discussed on page 2, lines 10-29 of the present Application, a single time-resolved study of the effect of a stimulus on a cell proteome would take an unacceptably long period to complete if the mass spectrometric analysis is performed serially. The claimed invention of the present Application addresses this problem by providing an interconnected array of parallel mass spectrometry systems and allocating the samples to the individual mass spectrometry system wherein each system analyzes a different one of the multiple samples. By concurrently analyzing individual samples of a large set of multiple, related samples, proteomic analysis may be achieved in a time-effective manner.

Furthermore, one of ordinary skill in the art would not have any motivation to modify the Chang apparatus such that each one of its mass analyzers analyzes a different sample. As discussed above, the problem solved by the Chang apparatus relates to the timing of mass selective scans performed by a mass spectrometer relative to the elution of analyte substances from a chromatography column or other separation device. The Chang apparatus addresses this problem by employing two analyzers, operating in different modes, which concurrently analyze ions produced from a single sample. The detection of an eluting chromatographic peak by one of the mass analyzers, which operates in TIC or SIM mode, triggers the initiation of a mass-sequential scan by the other mass analyzer. The Chang invention requires that the two analyzers concurrently analyze a single common sample; the "triggering" function that lies at the heart of the Chang invention would simply not be possible if the two analyzers concurrently analyzed different samples.

In sum, claim 1 is submitted to be patentable over Chang because Chang neither discloses nor suggests a parallel array of mass spectrometry systems wherein each mass spectrometry system analyzes a different one of the multiple protein samples derived from separation of a complex protein mixture. Therefore, withdrawal of this rejection is believed to be in order.

Claims 2, 5-18, and 38-45, which depend directly or indirectly from claim 1 and inherit all of the limitations thereof, are submitted to be patentable over Chang for at least the reasons advanced above in connection with claim 1.

Independent claim 22 was rejected under §102(b) as being anticipated by Chang. Applicants traverse this rejection as applied to the amended claim for substantially the same

reasons discussed above in connection with claim 1. More specifically, claim 22 now recites a step of allocating multiple protein samples among mass spectrometry systems in a parallel array of systems "such that each mass spectrometry system analyzes a different one of the multiple protein samples." Again, Chang does not disclose or suggest a parallel array of mass spectrometry systems wherein each system analyzes a different sample; Chang's invention requires concurrent analysis by different mass analyzers of a single sample.

Claims 23-28, which depend directly or indirectly from claim 22 and inherit all of the limitations thereof, are submitted to be patentable over Chang for at least the reasons advanced above in connection with claim 22.

Claims 1, 2, 5-18, and 22-45 were additionally or alternatively rejected under §103(a) as being unpatentable over Demirev in view of Chang. Applicants traverse this rejection as applied to the amended claims. In advancing this rejection, the Examiner notes that Demirev does not describe details of the mass spectrometry instrumentation employed for implementing the theoretical analysis technique described therein, but mentions certain performance factors that need to be considered, including efficiency and accuracy. The Examiner proceeds to argue that it would be obvious that the analytical approach of Demirev may require parallel mass spectrometers for its implementation, because (as stated on p. 7 of the Office Action):

> Demirev addresses difficulties in practical implementation of "massively parallel" mass spectrometry for detection, such as efficiency and accuracy, and Chang et al, also discussing difficulties in mass spectral identification of complex mixtures of ingredients, point to parallel mass spectrometer as being able to provide a significant advantage over conventional single mass spectrometer, for example in terms of resolution and sensitivity.

As understood by the Applicants, the underlying reasoning of the Examiner's argument appears to be as follows: (i) Demirev teaches that certain mass spectrometer performance criteria, including high sensitivity, are required or desirable for implementation of its technique for analyzing samples containing large numbers of peptides; (ii) Chang teaches a parallel mass spectrometer that provides advantages over conventional instruments in terms of sensitivity and resolution; and (iii) it would therefore be obvious to use the parallel mass spectrometer of Chang to implement the analytical approach of Demirev. However, even if one assumes that proper

motivation exists to combine the teachings of the Demirev and Chang references, such a combination does not anticipate or suggest the limitation, incorporated into all of the pending claims, of providing a parallel array of mass spectrometry systems wherein each mass spectrometry system analyzes a different one of the multiple protein samples derived from separation of a complex protein mixture. As discussed above, the Chang reference does not teach the use of mass spectrometry systems arranged in parallel for concurrent analysis of different samples. Chang instead teaches the use of two mass analyzers for concurrently analyzing a single sample in different operational modes in order to time the initiation of a mass scan by one analyzer based on the detection of a chromatographic peak by the other analyzer. Employing the Chang apparatus for the Demirev technique may result in achieving the desired sensitivity and/or resolution, but since analysis of different samples would still need to be conducted in serial fashion, the dramatic improvement in reducing the aggregate analysis time achieved by the present invention is not effected by the combination of Chang and Demirev.

In sum, claims 1, 2, 5-18, and 22-45 are submitted to be patentable over Demirev in view of Chang because neither Demirev nor Chang, taken individually or in combination discloses or suggests a parallel array of mass spectrometry systems wherein each mass spectrometry system analyzes a different one of the multiple protein samples derived from separation of a complex protein mixture. Therefore, withdrawal of this rejection is believed to be in order.

In view of the reasons set forth above, Applicants believe that the claims are now in condition for allowance, and passage of the Application to issue is requested. If the Examiner believes that a telephone conference may be useful to advance the prosecution of the Application, he is invited to contact the Applicants' undersigned representative.

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Respectfully submitted,

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